REMARKS

Claims 1-12 are withdrawn. Claims 16, 18, and 21 are canceled. Previously presented claims 14 - 15, 23 - 27, and 30; amended claims 13, 17, 19-20, 22, and 28-29; and new claims 31 - 36 are presented for continued examination. Amended claims 13, 17, 19-20, 22, and 28-29 and new claims 31 - 36 are fully supported by the specification as filed. For example, support for the "non-orally" limitation of amended claims 13, 22, and 29 is found, for example, at Examples 3 - 5 of the specification as filed. Support for the "both ... proteinous chemotherapeutic agent" limitation of Claim 22 is found, for example, at paragraph 10 of the specification as filed. Support for the "wherein said admixture is further comprised of" limitation of Claims 17 and 28 is found, for example, at paragraph 52 of the specification as filed. Support for the "galactomannan" limitation of Claims 13, 19-20, 22, and 29 is found, for example, at paragraph 152 of the specification as filed. Support for new claims 31-36 is found, for example, at paragraph 50 of the specification as filed. Accordingly, no new matter is being added.

Detailed Action

Applicant appreciates the Examiner's acceptance of terminal disclaimers as to any patent term extending beyond that of U.S. Patents Nos. 6,645,946; 6,982,255; and 7,012,068 (8/23/07 Office Action, p. 2).

In addition, Applicant appreciates the Examiner's withdrawal of certain objections enumerated at pages 2-3 of the 8/23/07 Office Action. In particular, Applicants appreciate the Examiner's recognition that "the claims are no longer drawn to a method of treating cancer" (8/23/07 Office Action at page 3) and that "the specification provides examples of suitable

ratios") (8/23/07 Office Action at page 3). Finally, Applicant appreciates the Examiner's recognition that "The prior art also discloses guar gum and galactomannan as pharmaceutical excipients that are used to improve the delivery to a wide variety of different therapeutic agents, usually orally." (8/23/07 Office Action at page 5).

Claim Rejections - 35 U.S.C. 112

Claims 25-27 - 35 U.S.C. 112, ¶2

Claims 25-27 stand rejected for lack of antecedent basis. In particular, the 8/23/07 Office Action asserts that "the base claim 22 specifically limits the chemotherapeutic agents to proteinous chemotherapeutic agents, while the dependent claims recite small molecule non-proteinous chemotherapeutic agents. Therefore the dependent claims lack antecedent basis in the base claim" (8/23/07 Office Action, pp. 3-4).

In response, Applicants have amended pending Claim 22 as follows:

22. (Currently Amended) A method for improving the biodistribution of both a chemotherapeutic agent and a proteinous chemotherapeutic agent in a body, comprising:

Obtaining an admixture of galactomannan, the chemotherapeutic agent and a the proteinous chemotherapeutic; and

Nonorally aAdministering to the body an effective amount of the admixture so as to improve the biodistribution of the chemotherapeutic agent and the proteinous chemotherapeutic agent in the body.

As amended, Claim 22 now provides antecedent basis for dependent claims further reciting subgroups of particular proteinous chemotherapeutic agents. Withdrawal of this grounds for rejection is respectfully requested.

Claims 17 and 28 - 35 U.S.C. 112, ¶2

Claims 17 and 28 stand rejected under 35 U.S.C. 112, second paragraph as indefinite. Specifically, it is the 8/23/07 Office Action's position that

> "These claims are drawn to a therapeutic method, yet they include the limitation that the method comprises leucovorin. A method comprises method steps, not compounds. It is not clear hat role the leucovorin plays in the method how it is to be used." (8/23/07 Office Action at p. 4).

In response, Applicant has amended Claims 17 and 28 so as to clarify that leucovorin is utilized as an additional component of the admixture of the pending method of treatment claims. Withdrawal of this grounds for rejection is respectfully requested.

Claim 28 - 35 U.S.C. 112, ¶¶1 and 2

Claim 28 stands rejected under 35 U.S.C. 112, first and second paragraphs for failure to comply with the enablement requirement and for introduction of new matter. Specifically, it is the 8/23/07 Office Action's position that "the instant specification as filed contains no description of such a combination, or of any activity of leucovorin that does not depend on co-administration with the nucloetide 5-flurouracil". (8/23/07 Office Action at page 12).

In response, Applicant has amended independent claim 22 (from which claim 28 depends) as follows:

22. (Currently Amended) A method for improving the biodistribution of both a chemotherapeutic agent and a proteinous chemotherapeutic agent in a body, comprising:

Obtaining an admixture of galactomannan, the chemotherapeutic agent and a the proteinous chemotherapeutic; and

Nonorally aAdministering to the body an effective amount of the admixture so as to improve the biodistribution of the chemotherapeutic agent and the proteinous chemotherapeutic agent in the body.

Claim 22 as amended now encompasses co-administration of leucovorin with a chemotherapeutic agent -- for example, 5 -FU. Withdrawal of this grounds for rejection is respectfully requested.

Claims 13, 19, 20, 22, 28, and 29: 35 U.S.C. 112, ¶1

Claims 13, 19, 20, 22, 28, and 29 stand rejected under 35 U.S.C. 112, ¶1 as not enabled for "every possible chemotherapeutic agent whatsoever" (8/23/07 Office Action at p.4). Applicants appreciate the Examiner's admission that the relative skill of those in the art is high (8/23/07 Office Action at page 6) It is the 8/23/07 Office Action's position that:

- The Breadth of the claims: The claimed invention is very broad, **encompassing any compound with utility as a cancer chemotherapeutic**, namely any substance whatsoever that can be administered so as to inhibit or kill cancer cells without killing the host." (8/23/07 Office Action at p. 6)(emphasis added).

- "The Nature Of The Invention: The claimed invention is **a therapeutic method comprising administering two compounds**, one of which is a chemotherapeutic agent." (8/23/07 Office Action at p. 5)(emphasis added).

- "The State of The Prior Art. The prior art does not disclose the **full scope of all possible chemotherapeutic agents, or a way to discover and produce all such agents**" (8/23/07 Office Action at page 5)(emphasis added).

- "The relative skill of those in the art: The relative level of skill in the art is high. (8/23/07 Office Action, p. 6)

- "The predictability or unpredictability of the art: The treatment of cancer is highly unpredictable…Furthermore, the class of chemotherapeutic agents includes a wide variety of diverse chemical structures. Synthesis of novel compounds is a complex process of trial and error which is necessary in order to develop a workable synthetic scheme for any novel compound."

- "The amount of direction or guidance presented: The claimed specific galactomannans are described and disclosed to be obtainable from guar. **A wide variety of different chemotherapeutic agents are listed as being enhanced by this galactomannan**. No guidance is given that would enable one skilled in the art to **discover new chemotherapeutic agents, much less all possible new chemotherapeutic agents**." (8/23/07 Office Action, page 7)(emphasis added).

- "The presence or absence of working examples. The specification discloses a number of tests showing improvement in the efficacy and toxicity of 5-FU (5-fluorouracil) when administered with the claimed galactomannan…Note that lack of working examples is a critical factor to be considered" (8/23/07 Office Action at page 7 (emphasis added).

- "The quantity of experimentation necessary: One of ordinary skill in the art, in order to practice the claimed invention with the full range of chemotherapeutic agents beyond the meager number disclosed in the specification **would be required to test potential compounds *in vivo*"** (8/23/07 Office Action at page 7 (emphasis added)

Each of these positions is addressed in turn below.

Breadth Of The Claims And Nature Of The Invention:

The claims of the present invention are **not** directed to novel chemotherapeutic agents, and the Examiner's statement that "The claimed invention is very broad, encompassing any compound with utility as a cancer chemotherapeutic") (8/23/07 Office Action at page 6) is respectfully traversed. Rather, the instant claims are directed to co-administration of known chemotherapeutic agents with a novel adjuvant that facilitates increased bioavailability of the known chemotherapeutic agents. This increased biodistribution is enabled in the specification as filed.

The Examiner's recognition in the 8/23/07 Office Action that "the claims are no longer drawn to a method of treating cancer" (8/23/07 Office Action at page 3) is correct. As noted in the 8/23/07 Office Action, the pending claims encompass "a therapeutic method comprising administering two compounds, one of which is a chemotherapeutic agent" (8/23/07 Office Action at page 5). More specifically, the pending claims are directed to **co-administration of a chemotherapeutic agent or agents and galactomannan,** wherein co-administration results in **subsequent, improved biodistribution of the chemotherapeutic agent** in the body.

As previously noted in Applicant's Amendment in response to October 2, 2006 Office Action, support for "increased biodistribution" is found, for example, at at least paragraph 73 of the specification as filed, and means increased exposure of tissue (for example, liver, kidney, tumor, and plasma) to a chemotherapeutic or proteinous chemotherapeutic agent. More specifically, paragraph 73 of the specification as filed provides that "galactomannan may

increase cancer cell membrane fluidity and permeability as a result of galactose-specific interactions at the surface of the target cell." Paragraph 74 of the specification as filed notes that "Another possible mode of action for the polysaccharide like galactomannan may involve its interaction with some regulatory sites in a biological system, for example, if those sites are governed by galactose-specific residues, such as galectins." Finally, paragraphs 185 - 186 of the specification as filed sum up the biodistribution study (Exhibit 6) of the specification as filed:

> In the presence of 5-FU the amount of GM in the tumor increases, and stays increased in the course of clearance of GM; and
>
> In the presence of 5-FU the amount of GM in the liver decreases, and stays decreased in the course of clearance of GM.
>
> That is, **5-FU and GM work in a synergism** when delivered into the tumor.

'508 specification, paragraphs 00185 – 00187 (emphasis added).

The claimed invention is directed to a **galactomannan co-administered with a chemotherapeutic agent, thereby increasing the biodistribution of the chemotherapeutic agent.** The relevant enablement analysis is whether the specification enables one of ordinary skill in the art to use the novel galactomannan composition in conjunction with a compound having chemotherapeutic properties -- not whether the specification enables discovery of new agents or classes of chemotherapeutic compounds. Accordingly, the presented claims encompass all chemotherapeutic agents **capable of synergistically increasing bioavailability when co-administered with galactomannan,** not all agents with utility as a cancer chemotherapeutic. Withdrawal of this grounds for rejection is respectfully requested.

The Claimed Invention Is Enabled In Light Of The Prior Art.

Applicants respectfully traverse the 8/23/07 Office Action's statement that "The prior art does not disclose the full scope of all possible chemotherapeutic agents, or a way to discover and produce all such agents (8/23/07 OA at p. 5). As noted above, the claimed invention is not a novel chemotherapeutic agent but the co-administration of a chemotherapeutic agent with a novel galactomannan composition. The Examiner contends that the use of "all possible chemotherapeutic agents" is not taught in the present application. This contention is not supported by the text. For example, paragraphs 0043, 0044, 0053, 0059-0071 describe the use of numerous chemotherapeutics that my be co-administered with galactomannan so as to increase bioavailability. These chemotherapeutic agents are well known in the art and their characteristics, including indications, are well appreciated by those of ordinary skill in the art.

The specification as filed also teaches (for example, at Example 2) the manufacturing process yielding the novel galactomannan compound of the claimed invention. In light of the fact that it is the synergistic effect of co-administration of the novel galactomannan compound and a chemotherapeutic that facilitates increased chemotherapeutic bioavailability, Applicant respectfully submits that the claim considered as a whole (novel adjuvant combined with a known chemotherapeutic) is fully enabled by the specification as filed. *See, e.g.* MPEP 2164.08 "The Examiner should determine what each claim recites and what the subject matter is when the claim is considered as a whole, not when its parts are analyzed individually."

The Relative Skill Of Those In The Art is High

Applicants appreciate the Examiner's determination that that the level of skill of those in the art is high. (8/23/08 Office Action at page 6). For this reason, one of ordinary skill in the art

would be familiar with the full scope of chemotherapeutic agents disclosed in the specification as filed.

The Relevant Art Is Not Highly Unpredictable

Page 6 of the 8/23/07 Office Action states that "The treatment of cancer is highly unpredictable…Synthesis of novel compounds is a complex process of trial and error which is necessary in order to develop a workable synthetic scheme for any novel compound." (8/23/07 Office Action at page 6). Applicants respectfully traverse this grounds for rejection. As previously noted, the Examiner has admitted that "the claims are no longer drawn to a method of treating cancer" (8/23/07 Office Action at page 3). As the claims are drawn to increasing the bioavailability of a chemotherapeutic agent, Applicants respectfully submit that it is the capability of a chemotherapeutic agent to synergistically interact with the claimed novel polysaccharide – not the structure or mechanism of action of the particular co-administered chemotherapeutic agent—that is the focus of the invention as claimed. Further, galactomannan is a polymeric structure comprising a mannose backbone with galactose residues stemming from the backbone. The Examiner suggests that it is difficult to predict whether other chemotherapeutics (other than 5-FU) will also synergistically interact with the novel galactomannan so as to produce the claimed synergistic increased bioavailability. A review of the specification as filed reveals that such unpredictability is unlikely. 5-FU was employed simply as an example and should not be construed as exhausting the possible drug combinations with galactomannan. The use 5-FU demonstrated the utility of combining a chemotherapeutic agent with galactomannan and should not be construed as limiting. A skilled artisan will appreciate that if 5-FU in combination with galactomannan resulted in increased bioavailability

of the chemotherapeutic agent, then other chemotherapeutics will most likely benefit from the presence of galactomannan.

Mere Quantitative Experimentation Is Not Undue In Light Of The Guidance And Ease Of Carrying Out The Required Assay Needed To Determine Increased Bioavailability

The 8/23/07 Office Action states at page 6 that "No guidance is given that would enable one skilled in the art to discover new chemotherapeutic agents, much less all possible new chemotherapeutic agents", and further states that "lack of working examples is a critical factor to be considered." (Id.). Applicants respectfully traverse this basis for rejection. As noted above, new chemotherapeutic agents are not claimed in this application. Rather, the relevant analysis is whether guidance is given that would enable one skilled in the art to discover whether known chemotherapeutic agents would synergistically increase bioavailability when co-administered with a claimed, novel polysaccharide, without undue experimentation. The 8/23/07 Office Action has not demonstrated why such experimentation would be undue. Indeed, the specification as filed provides routine experimental protocols for measuring *in vivo* bioavailability (for example, Example 6 of the specification as filed) as well as routine experimental protocols for ascertaining the synergistic effects of claimed polysaccharide / known chemotherapeutic coadministration as compared to administration of claimed polysaccharide or known chemotherapeutic alone (see, for example, Examples 3, 4, and 11 of the specification as filed). "Undue experimentation" is not a mere measurement of time and effort needed to complete the needed tests; if the testing protocol is routine, time and effort are immaterial. This is the case for the instant application.

Further, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. *See, e.g.* MPEP 2164.08; *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As the specification as filed provides both assays for determining bioavailability and lists of representative known chemotherapeutic agents whose bioavailability may be

increased by co-administration with a novel polysaccharide, determining whether a given chemotherapeutic agent's bioavailability is synergistically increased via co-administration with a novel polysaccharide is a matter of routine. *See MPEP 2164.08,* reproduced above; MPEP 2164.06 ("Time and difficulty of experiments are not determinative if they are merely routine."). Withdrawal of this grounds for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. 102

Klyosov '946 - Claims 13-15, 19, 20, and 25-27

Claims 13-15, 19, 20, and 25-27 stand rejected under 35 U.S.C. 102(e) as anticipated by Klyosov et. al (US patent 6645946). In response, Applicants will submit a request for change of inventorship in which Eli Zomer, Ph. D. is removed as a named inventor as to claims directed to a method of treatment utilizing an admixture including galactomannan. In addition, Anatole Klyosov, Ph.D. was added as an inventor to the instant application pursuant to the Request to Correct Inventorship filed in the instant case on September 15, 2005.. In light of the request for change of inventorship that will be submitted and the fact that, upon grant of the request, Klyosov '946 will no longer constitute a 102(e) reference (see MPEP 2136.04), withdrawal of this basis for rejection is respectfully requested.

Lee '494 - Claims 13-15, 25-27

Claims 13-15 and 25-27 stand rejected under 35 U.S.C. 102(b) as being anticipated by United States Patent No. 6,413,494, issued to Lee et. al. ("Lee '494"). The 8/23/07 Office Action stated that "Lee et. al. discloses a composition and pharmaceutical dosage form for delivering an orally administered drug specifically to the colon, thereby improving its

biodistribution in the body…Therefore administring the fluorouracil-containing composisitons of Lee et. al. **is reasonably considered to be a method comprising the same steps as**, and thus anticipating, the claimed invention (8/23/07 Office Action at p. 13 (emphasis added).

This position is without merit in light of the amendments to the instant claims. Anticipation under 35 U.S.C. §102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Rockwell Int'l Corp. v. United States,* 147 F.3d 1358, 1363 (Fed. Cir. 1998). If the prior art reference fails to disclose even one limitation of the claimed invention, then the claim is not anticipated. *Structural Rubber Prods. Co. v. Park Rubber Co.,* 749 F.2d 707, 715 (Fed. Cir. 1984); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.,* 750 F.2d 1569, 1574 (Fed. Cir. 1984)).

Claims 13-15 and 25-27, as amended, require **nonoral** administration of an admixture of the claimed galactomannan compound and are not anticipated by the disclosure of Lee '494. Lee '494, in contrast, discloses use of "a colon specific drug delivery system (is designed such that it) remains intact in stomach and small intestine but releases encapsulated drugs only in colon." (Lee '494 col. 1, ll. 37-40). Indeed, the portion of the specification cited by the Examiner reemphasizes that "An object of the present invention is to provide a composition and pharmaceutical dosage form for delivering a drug, wherein such dosage form is orally-administered for specifically administering the drug to the colon of a subject in need thereof." (Lee '494 col. 4, ll. 32-36). Further, Lee '494 teaches dissolution / disintergration of the galactomannan disclosed in the specification.

Lee '494 also does not disclose the limitation of increasing biodistribution as found in the instant claims. Lee '494 does not disclose passage of galactomannan into the bloodstream; nor

does Lee '494 disclose any synergistic effect of increased biodistribution of a chemotherapeutic agent, nor any increase in cancer cell membrane fluidity and permeability or interaction with some regulatory sites as a result of galactose-specific interactions at the surface of the target cell. As Lee '494 does not teach or suggest all limitations of 13-15 and 25-27, as amended, withdrawal of this grounds for rejection is respectfully requested.

Simard '131 - Claims 13-15, 22, 25-27, and 29

Claims 13-15, 22, 25-27, and 29 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application No. 2006/0057131 ("Smiard '131"). The 8/23/07 Office Action stated that "Simard et al. discloses a biodegradable and non-toxic malleable protein matrix for delivering pharmaceuticals. (p. 2, paragraphs 0020-0023)...This matrix can be used in drug tablets to produce a tablet **that hydrates slowly and protects the incorporated agent while passing through the stomach**" (8/23/07 Office Action at p. 13-14)(emphasis added).

This position is without merit in light of the amendments to the instant claims. Anticipation under 35 U.S.C. §102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Rockwell Int'l Corp. v. United States,* 147 F.3d 1358, 1363 (Fed. Cir. 1998). If the prior art reference fails to disclose even one limitation of the claimed invention, then the claim is not anticipated. *Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 715 (Fed. Cir. 1984); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574 (Fed. Cir. 1984)).

Claims 13-15 and 25-27, as amended, require **nonoral** administration of an admixture of the claimed galactomannan compound and are not anticipated by the disclosure of Simard '131.

Page 2, paragraphs 0020-0023 and the examples of Simard '131 (including at least Examples 18-22 and 25) teach oral administration of the disclosed compounds.

Nor does Simard '131 disclose the limitation of increasing biodistribution as found in the instant claims. Simard '131 does not disclose passage of galactomannan into the bloodstream; nor does Simard '131 disclose any synergistic effect of increased biodistribution of a chemotherapeutic agent, nor any increase in cancer cell membrane fluidity and permeability or interaction with some regulatory sites as a result of galactose-specific interactions at the surface of the target cell. As Simard '131 does not teach or suggest all limitations of 13-15 and 25-27, as amended, withdrawal of this grounds for rejection is respectfully requested.

Boving '183 - Claims 13, 22-24, 29, 30

Claims 13, 22-24, 29, and 30 stand rejected under 35 U.S.C. 102(b) as anticipated by PCT international publication no. WO2004024183 ("Boving '183"). The 8/23/07 Office Action stated that "The **ghrelin antigen can be coupled to a polyhydroxypolymer** (p. 44, lines 25-34). Preferred polyhydroxypolymers include guar, which is a galactomannan having the characteristics of the claimed invention, as disclosed on p. 24 of the instant specification (p. 46, lines 1-5).....This method comprises the same steps as the claimed invention, **administering the same compounds** to a subject." (8/23/07 Office Action at pp. 14-15)(emphasis added).

This position is without merit. The polyhydroxypolymer compositions disclosed by Boving '183 are not the "same compounds" claimed in the instant application. Rather, the Boving '183 polyhydroxypolymer compounds are coupled to a ghrelin antigen or other chemical entity. *See,* for example, Boving '183 at page 21, lines 17-22:

> Preferred embodiments of covalent coupling of the ghrelin polypeptide to pharmaceutically acceptable polyhydroxypolymers such a carbohydrates involve the use of at least one ghrelin polypeptide and at least one foreign T-helper epitope which are coupled *separately* to the polyhydroxypolymer (*i.e.* the foreign T-helper epitope and the ghrelin polypeptide are not fused to each other but rather bound to the polyhydroxypolymer which then serves as a carrier backbone).

Withdrawal of this grounds for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. 103

Claims 19 and 20 - 103(a) over Lee '494

Claims 19 and 20 stand rejected under 103(a) over Lee '494. In light of the fact that Lee '494 does not teach or suggest all limitations of the parent claim from which Claims 19-20 depend (see above), withdrawal of this grounds for rejection is respectfully requested.

Claims 19 and 20 - Simard '131

Claims 19 and 20 stand rejected under 103(a) over Simard '131. In light of the fact that Simard '131 does not teach or suggest all limitations of the parent claim from which Claims 19-20 depend (see above), withdrawal of this grounds for rejection is respectfully requested.

Claims 19 and 20 - Boving '183

Claims 19 and 20 stand rejected under 103(a) over Boving '183. In light of the fact that Boving '183 does not teach or suggest all limitations of the parent claim from which Claims 19-20 depend (see above), withdrawal of this grounds for rejection is respectfully requested.

Claim 17 - Lee '494 in view of Jakobsen

Claim 17 stands rejected under 103(a) as being unpatentable over Lee '494 in view of Jakobsen. Jakobsen is cited by the 8/23/07 Office Action as teaching co-administration of 5- FU with leucovorin (See 8/23/07 Office Action at p. 19). In light of the fact that Lee '494 does not teach or suggest all limitations of the parent claim from which Claim 17 depends (see above), withdrawal of this grounds for rejection is respectfully requested.

Claim 17 - Simard '131 in view of Jakobsen

Claim 17 stands rejected under 103(a) as being unpatentable over Simard '131 in view of Jakobsen. Jakobsen is cited by the 8/23/07 Office Action as teaching co-administration of 5- FU with leucovorin (See 8/23/07 Office Action at pp. 19-20). In light of the fact that Simard '131 does not teach or suggest all limitations of the parent claim from which Claim 17 depends (see above), withdrawal of this grounds for rejection is respectfully requested.

Claim 17 - Lee '494 in view of Van de Bongard

Claim 17 stands rejected under 103(a) as being unpatentable over Lee '494 in view of Van de Bongard. Van de Bongard is cited by the 8/23/07 Office Action as teaching co-administration of 5- FU with leucovorin. (See 8/23/07 Office Action at pp. 20-21). In light of the fact that Lee '494 does not teach or suggest all limitations of the parent claim from which Claim 17 depends (see above), withdrawal of this grounds for rejection is respectfully requested.

Claims 13-15, 19, 20, 25-27 - Klyosov '946 in view of Jakobsen

Claims 13-15, 19, 20, and 25-27 stand rejected under 35 U.S.C. 103(a) over Klyosov '946 in view of Jakobsen. Jakobsen is cited by the 8/23/07 Office Action as teaching co-administration of 5- FU with leucovorin (See 8/23/07 Office Action at pp. 21-22). In light of the

request for change of inventorship that removes Klyosov '946 as a reference, withdrawal of this grounds for rejection is respectfully requested.

Objection – Double Patenting

Currently pending claims 13-15, 17, 19-20, and 22 stand rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over certain claims of U.S. Patents Nos. 6,645,946; 7,012,068; and 6,982,255. Pursuant to 37 CFR 1.321(c), Applicants agree to file a terminal disclaimer in order to disclaim any term of the patent issuing from this application past the expiration of U.S. Patents Nos. 6,645,946; 7,012,068; and 6,982,255, and will file terminal disclaimers herewith.

Rejection under 35 U.S.C. 112(1)—Undue Experimentation

Currently pending claims 13-15, 17, 19-20 and 22-25 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use an invention commensurate in scope with the claims. The Examiner states that "Claim 13-25 are rejected under 35 U.S.C., first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim with respect to treating any cancer in a subject broadly in claims 13 - 17 and 19 -25, and/or those numerous cancers listed in claim 18." (10/2/07 Office Action, pp. 7-8). The Examiner further states that "the specification fails to provide sufficient support of the broad use of the said admixture for treating numerous and varied cancers recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of

chemotherapeutic agents in the presence of galactomannan and cancers encompassed by the instant claims suitable to practice the claimed invention." (*Id.*, pp. 10-11). Applicants respectfully disagree.

In response, Applicants have amended independent claim 13 so as to specify that the claimed invention recites a method for "improving biodistribution of a chemotherapeutic agent in the body." Support for this amendment is found, for example, at paragraphs 73 - 74 of the application as filed and at Example 6 (paragraphs 170 - 189) of the application as filed. For example, "improved biodistribution" means increased exposure of tissue (for example, liver, kidney, tumor and plasma) to a chemotherapeutic agent. Such improved biodistribution can be measured, for example, by the methods described in Example 6 of the specification as filed.

Applicants respectfully submit that, although Applicants disagree with the Examiner, the amended claims directed to "improving biodistribution of a chemotherapeutic agent in the body" render this rejection moot. Withdrawal of this grounds for rejection is respectfully requested.

Rejection under 35 U.S.C. 112(2)—Indefiniteness

Currently pending claims 19-20 and 22-25 stand rejected under 35 U.S.C. 112(2) as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner has rejected claims 13-25 as indefinite, stating that "In all occurrences of the presented claims, in the absence of the specific ratio between galactomannan and other agents, render the claims indefinite wherein applicant fails to articulate the specific ratio, requisite to identifying the admixture having galactomannan and other agents.")(10/2/06 Office Action at pp. 11- 12). Applicants disagree.

Paragraph 10 of the specification as filed provides a specific range of suitable ratios for reducing toxicity, as shown below:

> In one aspect, the mixture in the formulation contains an amount of one or more polysaccharides and one or more chemotherapeutic agents in a ratio suitable for reducing any toxic side-effect in the subject. The polysaccharide to chemotherapy ratio could be in the range from 10:1 up to 1:10. With the 50,000 MW modified galactomannan the optimum ratio was in the range from 6:1 to 1:3. In another aspect, the mixture contains an amount of one or more polysaccharides and one or more chemotherapeutic agents in a ratio suitable for enhancing efficacy of chemotherapeutic effect for treating the cancer.

Applicants respectfully submit that, although Applicants disagree with the Examiner, the amended claims incorporate a specific range or ratios of galactomannan and other agents present in the admixture. The amendment thus renders this rejection moot. Withdrawal of this grounds for rejection is respectfully requested.

CONCLUSION

Claims 13-15, 17, 19-20 and 22-25 as amended herewith and new claims 26-30 are presented for continued examination. Early and favorable consideration on the merits is earnestly solicited. If any additional fee is due, the amount of such fee may be charged to Deposit Account No. 50-1561.

Respectfully submitted,
GREENBERG TRAURIG

Dated: February 26, 2008

By: /Barry J. Schindler/
Barry J. Schindler
Registration No. 32,938

Mailing Address:
GREENBERG TRAURIG LLP
Met Life Building
200 Park Avenue
New York, NY (212) 801 -2244
Facsimile: (212) 801 - 6400